

Methodology of Isoproterenol-Tilt Table Testing in Patients With Syncope

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To assess the impact of isoproterenol, duration of tilt, symptom development and hemodynamic changes on the outcome of tilt table tests, 100 patients with syncope underwent successive 80° head-up tilt for 10 min during infusions of 0, 2 and 5 µg/min of isoproterenol. All 15 patients with another cause of syncope had a normal test result and 66 (78%) of the 85 patients with syncope of unknown origin had a test that resulted in syncope or presyncope. Isoproterenol was required to produce syncope or presyncope in >90% of positive tests and 66% to 80% of positive tests required a dose of 5 µg/min of isoproterenol.

Without isoproterenol, symptoms did not develop until after ≥4 min of head-up tilt. With either 2 or 5 µg/min of isoproterenol, the half-time of symptom onset was 0.7 to 1.9 min and the rate of symptom development did not depend on the dose of isoproterenol. During syncope, the mean heart rate, systolic blood pressure

and rate-pressure product each decreased significantly from 132 ± 21 to 67 ± 25 beats/min, 117 ± 19 to 60 ± 16 mm Hg and 15.3 ± 2.9 to $4.2 \pm 2.2 \times 10^3$ mm Hg/min, respectively.

During presyncope, mean trough rate-pressure product ($5.5 \pm 2 \times 10^3$ mm Hg/min) was significantly higher ($p = 0.027$) than during syncope. Receiver-operating characteristic analysis showed that a trough rate-pressure product $\leq 9,000$ mm Hg/min best separated tests ending in syncope or presyncope from asymptomatic tests (positive predictive value 0.96 to 1.0, negative predictive value 0.91 to 0.94) regardless of isoproterenol dose.

These results 1) demonstrate the need for isoproterenol to induce syncope or presyncope within 5 min of head-up tilt, 2) indicate that presyncope can be used as an outcome, and 3) define an objective hemodynamic outcome variable.

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Tilt table testing holds considerable promise for the diagnosis of neuromediated syncope. Syncope occurs in ≥3% of adults (1) and until recently its cause could not be established in 50% to 85% of cases (1,2). However, the use of head-up tilt table testing has demonstrated that neurally mediated bradycardia and hypotension cause presyncope or syncope in most patients with heretofore undiagnosed syncope (3-6).

Despite the promise of this testing technique, several factors prevent it from being generally useful in the diagnosis of a syndrome that is not likely to be fatal (1,2) and that has a probable prevalence rate of ≥1%. Some of the current techniques are highly invasive, utilizing intraarterial catheters and often performed after electrophysiologic testing (4) or cardiac catheterization (6). The procedures used are often lengthy because they may involve up to six graded infusions of isoproterenol (4), each lasting up to 15 min. Tests without

isoproterenol may require 45 to 60 min of head-up tilt (3,5,7). As well, some tests result in presyncope rather than syncope and the diagnostic importance of this outcome is unclear. Finally, there is no standard against which the test can be judged and with which the syndrome can be diagnosed.

Given these considerations, our eventual goal is to develop a simple, rapid, uniform, one-stage tilt table test that does not use intraarterial monitoring and that is applicable for routine clinical use. To this end, we evaluated the contribution of several variables of isoproterenol-tilt table testing to the diagnosis of syncope. Specifically, we evaluated the contributions of isoproterenol infusion, duration of head-up tilt and changes in hemodynamic variables to the diagnostic outcome of the test. Finally, presyncope is a common test outcome of uncertain significance in patients with a history of syncope because it incompletely reproduces clinical symptoms. To assess the hypothesis that presyncope and syncope are equivalent test outcomes, we compared the first three variables in tests that ended in presyncope or syncope.

Methods

Study patients. The study group consisted of 100 sequential patients referred for assessment of syncope who underwent tilt table testing if they had previously had 1) two or more syncopal episodes, 2) one syncopal episode and four or more presyncopal episodes, or 3) a single episode of syncope

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causing serious injury. Patients with structural heart disease, documented ventricular tachycardia or bifascicular block also underwent ambulatory electrocardiography and programmed electrical stimulation with use of a previously described protocol (8). Tilt table tests and electrophysiologic studies were performed on separate days. No patient underwent tilt table testing while taking a beta-adrenoceptor blocking agent, disopyramide or a drug with anticholinergic activity (9). All patients gave informed consent to the procedure.

Tilt table tests. Patients underwent tilt table testing in a quiet room after they had fasted for 4 to 8 h. They were comfortably restrained on an electric tilt table. Instrumentation consisted of a peripheral intravenous cannula and automatic and manual sphygmomanometric blood pressure cuffs. A modification of a previously described (4,6) tilt table protocol was used. Initially, patients received an infusion of 5% dextrose in water for 5 min while supine, then for 10 min in an 80° head-up position. The test was ended if syncope developed but otherwise proceeded to isoproterenol infusion. The second stage consisted of an infusion of 2 µg/min of isoproterenol for 5 min with the patient supine, followed by a similar infusion for 5 min with the patient in the 80° head-up position. The test was ended if syncope developed but proceeded to the last stage in the absence of symptoms. However, if presyncope developed in the 1st 5 min of head-up tilt, the 2-µg/min isoproterenol infusion was continued until the development of syncope or to a total of 10 min. The last stage consisted of an infusion of 5 µg/min of isoproterenol for 5 min with the patient supine, followed by a similar infusion during 80° head-up tilt until the development of syncope or to a total of 10 min in the head-up position. Heart rate, blood pressure and symptoms were recorded each minute.

Definitions. Syncope was defined as a transient state of unconsciousness characterized by spontaneous recovery or recovery in the supine position. Presyncope was defined as a state of light-headedness that substantially reproduced the clinical presyncope of the patient and was usually associated with one or more symptoms of decreased vision, the sensation of hearing voices distantly, slow response times to verbal stimuli, nausea, vomiting or partial loss of postural tone. Isolated presyncope was defined as a subset of presyncope that did not lead to syncope during the stage of the tilt table test in which it developed.

Statistics. Results are expressed as mean values \pm SD. One-way analysis of variance was used to compare the differences between multiple groups. Student *t* tests (paired or unpaired) were used to compare differences between pairs of groups. The correlation of continuous variables between groups was determined by linear regression analysis. The null hypothesis was rejected at a level of $p < 0.05$. Receiver-operating characteristic analysis was performed as described by Metz (10).

Table 1. Clinical Characteristics of 85 Patients With Syncope of Unknown Origin Undergoing Tilt Table Testing

	Test Outcome			p Value (ANOVA)
	Negative	Presyncope	Syncope	
No.	19	25	41	
% Male	57	32	45	—
Age (yr)	53 \pm 17	45 \pm 22	34 \pm 18	<0.001*
Syncope episodes (no.)				
Mean \pm SD	262 \pm 1,027	312 \pm 1,208	95 \pm 325	NS
Median	6	17	5	—
Duration of symptoms (min)				
Mean \pm SD	88 \pm 145	88 \pm 124	49 \pm 77	NS
Median	25	24	18	—

*Presyncope vs. syncope, $p < 0.02$; negative vs. syncope, $p < 0.001$. NS = $p > 0.05$.

Results

Clinical characteristics (Table 1). Of the 100 patients with syncope who underwent tilt table testing, 66 had a test that ended in presyncope or syncope. Of these tests, 41 ended in syncope and 25 in presyncope. Patients with a normal test result tended to be older (53 \pm 17 years) than patients with presyncope (45 \pm 22 years) and were significantly older than patients with syncope (34 \pm 18 years). The groups had a similar gender distribution and a similar number of syncopal episodes. The mean \pm SD and median number of syncopal episodes reflect the fact that although a few patients had a very large number of syncopal episodes, 50% of the patients had five or fewer episodes. Patients in all three groups had a similar duration of symptoms. Thus, the only significant difference between the groups was age, patients with a normal test result being significantly older than patients with a test ending in syncope ($p < 0.001$).

Diagnostic accuracy. Determining the specificity of this tilt table test was not a goal of the study protocol. However, none of the 15 patients with syncope due to other known causes (inducible ventricular tachycardia in 4, carotid sinus syndrome in 3, His-Purkinje disease in 3, cough syncope in 1, beta-adrenergic blocker overdose in 1, sinus arrest in 1, rapid atrial fibrillation in 1 and epilepsy in 1) had a test that resulted in clinically relevant presyncope or syncope. Of the 85 patients with syncope of unknown origin, 66 had a test ending in presyncope or syncope. Thus, the apparent yield of this protocol in the diagnosis of syncope of unknown origin is 78% and no patient with syncope due to other causes had a positive tilt test result.

Contribution of each stage to symptomatic outcome (Tables 2 and 3). Our eventual goal is to develop a tilt test that uses a single infusion of isoproterenol. Therefore, the relative diagnostic contributions of each of the three isoproterenol doses (none and 2 and 5 µg/min) were assessed with four measures: the first stage during which symptoms developed, the stage during which syncope occurred, the last symptomatic stage of the test and the time dependence of symptom

Table 2. Contribution of Each Isoproterenol Dose to Diagnostic Outcome in 66 Patients With Syncope or Presyncope on Tilt Table Testing

Isoproterenol Dose ($\mu\text{g}/\text{min}$)	First Onset of Symptoms		Occurrence of Syncope		Last Diagnostic Stage	
	No.	%	No.	%	No.	%
0	5	8	4	10	4	6
2	17	26	9	22	9	14
5	44	67	28	68	53	80
Total	66	100	41	100	66	100

development with and without isoproterenol (Table 2, Fig. 1). First, symptoms of presyncope or syncope occurred in only 5 (8%) of 66 patients in the absence of isoproterenol and in only 17 (26%) of 66 patients given 2 $\mu\text{g}/\text{min}$ of isoproterenol. In 44 (67%) of the 66 tests that ended in presyncope or syncope, the patient first developed symptoms during a 5- $\mu\text{g}/\text{min}$ infusion of isoproterenol, demonstrating the importance of this dose in eliciting symptoms.

Second, we determined the number of patients at each stage who developed syncope. Among 41 patients whose test ended in syncope, syncope occurred in the absence of isoproterenol in 4 and during the 2- $\mu\text{g}/\text{min}$ infusion of isoproterenol in 9. The other 28 patients (68%) developed syncope with 5 $\mu\text{g}/\text{min}$ of isoproterenol, demonstrating the importance of this dose of isoproterenol in eliciting syncope.

Third, we determined the incidence of each stage at which a diagnostically positive test ended. By design, the tilt table test could not be ended as a result of presyncope that occurred in the absence of isoproterenol or in the presence of only 2 $\mu\text{g}/\text{min}$ of isoproterenol. Tests were allowed to end when presyncope occurred only if the patient had received 5 $\mu\text{g}/\text{min}$ of isoproterenol for a 10-min head-up tilt. Of 66 tests ending in presyncope or syncope, 4 (6%) ended with syncope in the absence of isoproterenol, 9 (14%) ended in the presence of 2 $\mu\text{g}/\text{min}$ of isoproterenol and 53 (80%) ended in the presence of 5 $\mu\text{g}/\text{min}$ of isoproterenol.

Finally, we compared the rate of development of presyncope in 57 patients who developed presyncope or syncope either without isoproterenol ($n = 5$) or with 5 $\mu\text{g}/\text{min}$ of isoproterenol ($n = 52$). During the 1st 5 min of head-up tilt, only 1 patient developed presyncope without isoproterenol, whereas 50 (96%) of 52 patients who developed symptoms with 5 $\mu\text{g}/\text{min}$ of isoproterenol did so within 5 min of assuming the head-up position. Presyncope in this group developed without a lag (Fig. 1A) and reached a plateau with a time course that was fit by a monoexponential equation ($r = -0.98$) (Table 3).

Thus, head-up tilt with an infusion of 5 $\mu\text{g}/\text{min}$ of isoproterenol makes the greatest contribution to a positive test, whether this is assessed at the stage during which symptoms first occurred (66%), the stage during which syncope occurred (68%), or the stage at which the test ended (80%) or by the time dependence of symptom development.

Duration of head-up tilt and symptom development. The monoexponential time course for the development of presyncope (Fig. 1) has two potential implications for the development of a tilt test with a single infusion of isoproterenol. First, it suggests that the effect of various doses of isoproterenol on the rate of symptom development could be determined by comparing the half-times of symptom onset during these different infusions of isoproterenol. Second, it affords the opportunity to optimize the duration of head-up tilt to yield a maximal number of positive tests with a minimal duration of tilt.

Figure 1 shows the time course of symptom development in the 52 patients who were symptomatic during head-up tilt with an infusion of 5 $\mu\text{g}/\text{min}$ of isoproterenol. The rate of symptom development is displayed for four groups of patients (28 patients with presyncope that was followed by syncope, 24 patients with isolated presyncope, all 52 symptomatic patients with presyncope and 28 patients with syncope). All symptoms developed with an apparent monoexponential time course. Syncope developed with a half-time of 1.9 min, including an apparent lag of 0.7 min. Presyncope in the entire study group followed an apparent monoexponential

Table 3. Time-Dependence of Symptom Development During Isoproterenol Infusion in 52 Patients

Symptom	Isoproterenol, 2 $\mu\text{g}/\text{min}$			Isoproterenol, 5 $\mu\text{g}/\text{min}$		
	No.	r Value	Half-Time to Symptom Onset (min)	No.	r Value	Half-Time to Symptom Onset (min)
Presyncope if syncope ensues	9	-0.98	1.0	28	-0.99	0.7
Syncope	9	-0.97	1.7	28	-0.95	1.5
Isolated presyncope	8	-0.98	1.8	24	-0.96	1.3
All presyncope	17	-0.97	1.5	52	-0.98	1.2

The time dependence of symptom development during isoproterenol infusion and head-up tilt are derived from the data presented in Figure 1 and other related data. The correlation coefficient (r) describes the fit of the relevant data to a linear regression analysis of the equation $x = a(1 - e^{-bx})$, where x represents the number of symptomatic patients, a represents the total number of patients and t represents the duration of head-up tilt in minutes. Curves were not forced to pass through the origin $x = 0, t = 0$. The half-time required for development of symptoms in susceptible patients is also derived from this equation.

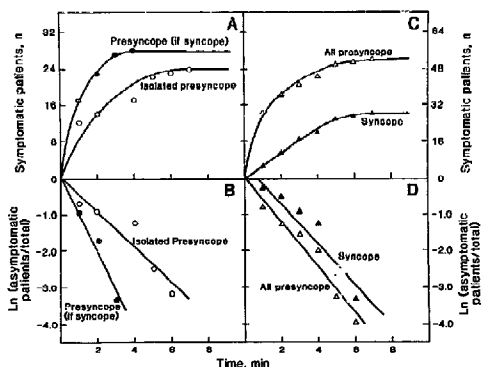


Figure 1. Time course of the onset of symptoms during head-up tilt with infusion of 5 μ g/min of isoproterenol. In the bottom panels, curves are fit to the data with the monoexponential equation described in Table 4. Ln = natural logarithm.

nential curve with a half-time of 1.2 min, although this curve was composed of the curves of two subgroups: one with isolated presyncope (half-time 1.5 min) and another with presyncope followed by syncope (half-time 0.7 min). In these subgroups, the onset of symptom development during an infusion of 2 μ g/min of isoproterenol followed a similar time course (data not shown) and is summarized in Table 3.

The fit of the time course of symptom development to monoexponential curves facilitates comparisons of both the dependence of symptom development on isoproterenol dose and the rate of development of symptoms in the various groups (Table 3). For example, in patients who develop syncope, the rate of onset of presyncope is similar during both 2 μ g/min (half-time 1 min) and 5 μ g/min (half-time 0.7 min) of isoproterenol. Similarly, isolated presyncope develops more slowly than does presyncope that progresses to syncope, whether this is assessed during infusion of 2 μ g/min (half-time 1.8 vs. 1 min) or 5 μ g/min (half-time 1.5 vs. 0.7 min) of isoproterenol.

Hemodynamic comparison of syncope and isolated presyncope (Table 4). Heart rate, systolic blood pressure and rate-pressure product each decreased markedly and significantly in tests ending in syncope or in isolated presyncope in the presence of 5 μ g/min of isoproterenol, but not in tests ending asymptotically. Compared with tests ending in syncope, those ending in presyncope were characterized by a significantly smaller decrease in heart rate (syncope vs. presyncope, $p = 0.01$) and rate-pressure product (syncope vs. presyncope, $p = 0.027$). Thus, the presyncopal state is associated with hemodynamic changes that are slightly but significantly less disturbed than those in the syncopal state. These data support the use of presyncope that is similar to the patient's clinical presyncope as a test outcome, but

suggest the potential usefulness of objective hemodynamic outcome variables.

Hemodynamic measures of test outcome. To develop objective hemodynamic measures that would serve as dichotomous values to classify test outcome as normal or abnormal, we first compared the reductions in heart rate, systolic blood pressure and rate-pressure product between patients with asymptomatic tests and patients who developed frank syncope while receiving 5 μ g/min of isoproterenol (Fig. 2). There were marked and significant differences in the distributions of all three variables between the 28 tests ending in syncope and the 34 tests ending asymptotically. These data suggest that dichotomous values for trough heart rate, systolic blood pressure and rate-pressure product might discriminate between tests ending without symptoms or with syncope. Accordingly, receiver-operating characteristic analysis (10) of these three measures was performed. A negative test was defined as one with neither presyncope nor syncope and a positive test as one ending in syncope during an infusion of 5 μ g/min of isoproterenol.

The sensitivity and specificity of various trough heart rates, systolic blood pressures and rate-pressure products were determined and the results of conventional receiver-operating characteristic analysis are shown in Figure 3A. The trough rate-pressure product appears to best discriminate between tests ending with syncope and tests ending without symptoms.

To determine whether this finding is applicable to other test conditions and outcomes, we performed a similar receiver-operating characteristic analysis in which positive tests were defined as those ending in isolated presyncope during infusion of 5 μ g/min of isoproterenol (Fig. 3B), tests ending in either syncope or isolated presyncope with

Table 4. Comparison of Hemodynamic Findings During Syncope, Isolated Presyncope and Asymptomatic Tests During Infusion of Isoproterenol ($1 \mu\text{g}/\text{min}$) in 86 Tests

	Symptomatic Outcome			p Value (presyncope vs. syncope)
	Normal	Isolated Presyncope	Syncope	
Heart rate (beats/min)				
Peak	129 \pm 17	132 \pm 17	132 \pm 21	NS
Trough	136 \pm 20	85 \pm 22	67 \pm 25	0.01
p Value (peak vs. trough)	NS	<0.001	<0.001	—
Blood pressure (mm Hg)				
Peak systolic	127 \pm 27	126 \pm 30	117 \pm 19	NS
Trough systolic	118 \pm 28	65 \pm 14	60 \pm 16	NS
p Value (peak vs. trough)	NS	<0.001	<0.001	—
Rate-pressure product (mm Hg/min $\times 10^3$)				
Peak	16.2 \pm 3.6	16.6 \pm 3.5	15.3 \pm 2.9	NS
Trough	16 \pm 4.5	5.5 \pm 2	4.2 \pm 2.2	0.027
p Value (peak vs. trough)	NS	<0.001	<0.001	—

Hemodynamic findings in the third head-up tilt stage in 34 asymptomatic tilt table tests, 24 tests ending in isolated presyncope and 28 tests ending in syncope are compared. In symptomatic tests, peak and trough refer to findings preceding and during symptoms. In asymptomatic tests, peak and trough refer to findings in this stage during the 1st and 10th min of head-up tilt. Four patients with syncope had a trough blood pressure too low to be recorded, and one patient with syncope dislodged her electrocardiographic leads; these data are not included. The statistical significance of compared results was determined by the Student *t* test. NS = *p* > 0.05.

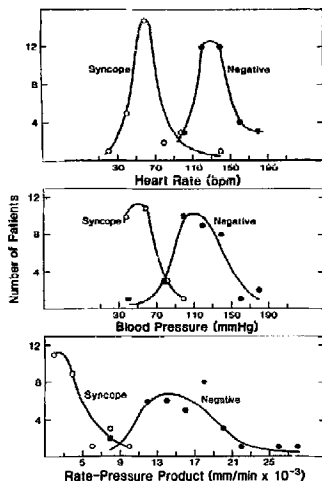
5 $\mu\text{g}/\text{min}$ of isoproterenol (Fig. 3C) and tests resulting in either syncope or isolated presyncope with 2 $\mu\text{g}/\text{min}$ of isoproterenol (Fig. 3D). The trough rate-pressure product best discriminated between negative and positive test results, regardless of which symptom was defined prospectively as positive. The data in Table 5 demonstrate the high positive and negative predictive values (0.91 to 1.0) of a trough rate-pressure product $\leq 9,000$ mm Hg/min.

Discussion

The principal conclusions of this study are that 1) an infusion of 5 $\mu\text{g}/\text{min}$ of isoproterenol is required for symptom development or diagnosis in 66% to 80% of tests, depending on when the test is judged to be positive; 2) a head-up tilt test lasting only 5 min is sufficient to induce symptoms in 93% of a susceptible group of patients; 3) a decrease in rate-pressure product to $\leq 9,000$ mm Hg/min accurately identifies both normal and abnormal test results; and 4) isolated presyncope resembles syncope, although the decrease in heart rate and rate-pressure product is significantly less severe. These results suggest the possibility of performing a very brief tilt table test with a single infusion of isoproterenol.

Diagnostic outcome of tilt table tests. The diagnostic characteristics of our tilt table protocol are similar to those of others, indicating that an exploration of tilt test variables with this protocol should be relevant and applicable. The proportion of positive tests in syncope patients in this study (78%) compares well with the proportion of positive tests in similar patients in other studies, whether isoproterenol was infused (as in the studies of Waxman et al. [6], 73%;

Figure 2. Heart rate, systolic blood pressure and rate-pressure product during head-up tilt with 5 $\mu\text{g}/\text{min}$ of isoproterenol. The hemodynamic values occurred during syncope in tests with a positive result or after 10 min of head-up tilt in tests with a negative result.



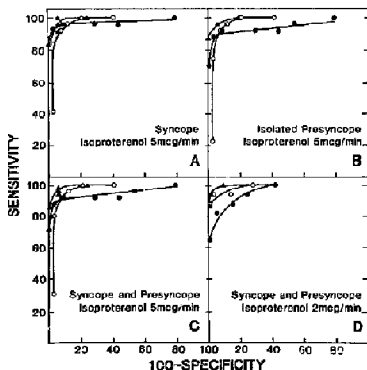


Figure 3. Receiver-operating characteristic analysis of trough heart rate (●), systolic blood pressure (○) and rate-pressure product (▲) as dichotomous hemodynamic variables. The data are from analyses similar to those of Figure 2. The symptoms against which these variables were tested were syncope during 5 µg/min of isoproterenol (A), isolated presyncope during 5 µg/min of isoproterenol (B), isolated presyncope and syncope during 5 µg/min of isoproterenol (C) and isolated presyncope and syncope during 2 µg/min of isoproterenol (D). Sensitivity and specificity are expressed in percent as is 100 minus specificity.

Pongiglione et al. [11], 80%; Almqvist et al. [4], 87%) or whether isoproterenol was not used (as in the studies of Fitzpatrick and Sutton [12], 74%; Abi-Samra et al. [3], 65%; Strömberg et al. [13], 38%). Similarly, the lack of ability to induce clinically relevant symptoms in all 15 patients with other causes of syncope compares well with the 85% to 100% specificity reported by others (4,6,12,13). However, several factors might influence the apparent specificity of these test protocols. For example, the degree of intravascular instrumentation alters the specificity of the test. Stevens (14)

showed that 52% of 81 asymptomatic subjects became syncopeal when head-up tilt table testing was conducted with intraarterial monitoring, but only 9% of 223 asymptomatic subjects became syncopeal during tilt table testing without intravascular monitoring. In addition, tilt table specificity may be related to age (15). Selecting patients in a predominantly older population as normal control subjects may overestimate the specificity of a protocol.

Evaluation of tilt table test conditions. The primary goal of this work was to assess some of the variables of the tilt table test that elicit a positive test outcome, both to better understand the technique and to define the conditions for a briefer single-infusion test. First, an isoproterenol infusion was necessary to produce a positive outcome in 90% to 92% of tests ending in either syncope or presyncope. This observation is in contrast to the data of Johnson et al. (16), who found that about 40% of patients who fainted during their study protocol did so in the absence of isoproterenol. It may be noteworthy that the tilt tests in that study (16) were associated with intraarterial cannulation. The role of isoproterenol in eliciting syncope is unknown; Waxman et al. (6) proposed that it increases contractility, thereby increasing left ventricular baroreceptor discharge.

Second, the monoexponential time course of the onset of symptoms with isoproterenol infusion allows an estimate of the optimal duration of the infusion. A head-up tilt with any effective dose of isoproterenol should elicit symptoms in 95% of susceptible patients within 5 min, and much longer tilts are clearly unnecessary.

Third, objective hemodynamic outcome variables were evaluated. These are necessary given the occasional uncertainty of the significance of isolated presyncope as a test outcome. A decrease in the rate-pressure product to $\leq 9,000$ mm Hg/min $\times 10^3$ accurately identified 96% to 100% of positive tests and 91% to 94% of negative tests whether syncope or presyncope was the symptomatic end point and regardless of isoproterenol dose. A potential limitation of use of this variable is that trough blood pressure could not be recorded in 4 of 41 tests ending with syncope and heart rate data were not obtained in 1 of 41 tests ending with syncope. None of these lost data occurred in patients without syncope, indicating that this measurement could be used in patients with presyncope or equivocal outcomes. The use of this variable has the advantage of assessing the decrease in both heart rate and blood pressure that characterizes neuro-mediated syncope (3-6).

Isolated presyncope as a test outcome. Finally, we assessed presyncope as a clinical outcome of the test. Our results show that isolated presyncope develops at a rate similar to that of syncope but is associated with slightly but significantly less profound decreases in heart rate and rate-pressure product. However, patients with isolated presyncope have values for heart rate, blood pressure and rate-pressure product below the diagnostic dichotomous values derived for syncope. Finally, the test reproduces the patient's particular symptoms of clinical presyncope. Thus,

Table 5. Predictive Values of a Decrease in Rate-Pressure Product to $\leq 9,000$ mm Hg/min

Symptoms	Isoproterenol Dose (µg/min)	Predictive Value	
		Positive	Negative
Syncope and presyncope	2	1.0	0.91
Syncope	5	0.96	0.94
Isolated presyncope	5	0.96	0.94
Syncope and presyncope	5	0.96	0.94

The positive and negative predictive values of a decrease in rate-pressure product to $\leq 9,000$ mm Hg/min for tests ending in syncope or isolated presyncope, or both, during isoproterenol infusion are presented. Patients whose blood pressure was too low to be recorded ($n = 4$ during syncope with 5 µg/min of isoproterenol) are not included in this analysis.

presyncope and syncope have similar time courses and hemodynamic changes and both substantially reproduce the patient's clinical symptoms. Both appear to reflect the same pathophysiologic changes, but it is unknown whether they have the same prognostic value.

Limitations. This study has several limitations. First, the limitations of test mechanics and patient selection have been discussed. Second, it may be that the results of infusing 5 $\mu\text{g}/\text{min}$ of isoproterenol are biased because of tachyphylaxis due to the preceding lower dose infusion. This study does not address this concern, which is the subject of ongoing work. Third, the reproducibility of this protocol is not addressed here. Previous data (17) have shown that the overall reproducibility is 79% to 90%. Finally, there is no reference standard for judging tilt table tests. Neuromediated syncope is diagnosed as a symptomatic outcome on a tilt table test, but the specificity of the test has not been defined in a large number of asymptomatic patients, nor has the sensitivity been defined in patients with documented hypotension or bradycardia, or both, occurring spontaneously. However, our work indicates the feasibility of a single-stage tilt table test that would facilitate the study of both the specificity of the test and the pathophysiologic changes occurring during the test.

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